PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

CALENDARED/CK
30 Day US IDS

To:
JEFFREY S. KUBINEC
GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080-4990

23 APR 03
DUE DATE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing (*day/month/year*) 19 MAR 2003

RECEIVED
MAR 24 2003
GENENTECH, INC.
LEGAL DEPT.

Applicant's or agent's file reference
P1824R1

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/US02/08057

International filing date (*day/month/year*)
14 March 2002 (14.03.2002)

Applicant
GENENTECH, INC.

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34, chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 *bis*.1 and 90 *bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US	Authorized officer
Commissioner for Patents Box PCT Washington, D.C. 20231	Stephen L. Rawlings, Ph.D.
Facsimile No. (703)305-3230	Telephone No. (703) 308-0196

Form PCT/ISA/220 (April 2002) *(See notes on accompanying sheet)*

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P1824R1	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US02/08057	International filing date (*day/month/year*) 14 March 2002 (14.03.2002)	(Earliest) Priority Date (*day/month/year*) 02 April 2001 (02.04.2001)
Applicant GENENTECH, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**
   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
   ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:
   ☐ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☐ furnished subsequently to this Authority in written form.
   ☐ furnished subsequently to this Authority in computer readable form.
   ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
2. ☐ **Certain claims were found unsearchable** (See Box I).
3. ☒ **Unity of invention is lacking** (See Box II).
4. With regard to the **title**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. ____
   ☐ as suggested by the applicant. ☒ None of the figures
   ☐ because the applicant failed to suggest a figure.
   ☐ because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/08057

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-5 and 9-19

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/08057

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61K 39/00, 39/395
US CL : 424/133.1, 138.1, 143.1, 181.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/133.1, 138.1, 143.1, 181.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	YE D et al. Augmentation of a humanized anti-HER2 mAb 4D5 induced growth inhibition by a human-mouse chimeric anti-EGF receptor mAb C225. Oncogene. 1999, Vol. 18, pages 731-738.	1-5 and 9-19
Y	MURPHY WJ et al. Antibodies to CD40 prevent Epstein-Barr virus-mediated human B-cell lymphomagenesis in severe combined immune deficient mice given human peripheral blood lymphocytes. Blood. 01 September 1995, Vol. 86, No. 5, pages 1946-1953.	1-5 and 9-19
Y	ILLIDGE T et al. Radioimmunotherapy in the pi-BCL1 B cell lymphoma model: efficacy depends on more than targeted irradiation alone. Cancer Biother Radiopharm. December 2000, Vol. 15 , No. 6, pages 581-591.	1-5 and 9-19
Y	JAKOBSON E et al. Agonistic propeties of anti-B cell antibodies purified on staphylococcal protein A may be due to contaminating protein A. J Immunol Methods. 31 July 1992, Vol. 152, No. 1, pages 49-57.	1-5 and 9-19
T	OTTAIANO A et al. CD40 activation as potential tool in malignant neoplasms. Tumori. September-October 2002, Vol. 88, No. 5, pages 361-366.	1-5 and 9-19

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
07 February 2003 (07.02.2003)	19 MAR 2003
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Stephen L. Rawlings, Ph.D. Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)

PCT/US02/08057

INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ZIEBOLD JL et al. Differential effects of CD40 stimulation on normal and neoplastic cell growth. Arch Immunol Ther Exp (Warsz). 2000, Vol. 48, No. 4, pages 225-233.	1-5 and 9-19
Y	Zhou ZH et al. An agonist anti-human CD40 monoclonal antibody that induces dendritic cell formation and maturation and inhbits proliferation of a myeloma cell line. Hybridoma. December 1999, Vol 18, No. 6, pages 471-478.	1-5 and 9-19
Y	Maloney DG et al. IDEC-C2B8: results of a phase I mulitple-does trial in patients with relapsed non-Hodgkin's lymphoma. J Clin Invest. October 1997, Vol. 15, No. 10, pages 3266-3274.	1-5 and 9-19

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-19, drawn to a method for treating a mammal having a neoplastic disorder, wherein said method comprises administering to said mammal a combination of a CD40 specific agent and a CD20 specific agent, and a composition comprising said combination.

Group II, claim(s) 20, drawn to a kit.

Group III, claim(s) 21-30, drawn to a method for a method for treating a mammal having an autoimmune disorder, wherein said method comprises administering to said mammal a combination of a CD40 specific agent and a CD20 specific agent, and a composition comprising said combination.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Claims 1 and 2 are generic to a plurality of distinct species of invention, wherein said neoplastic disease or disorder is selected from the group consisting of (a) lymphoma, (b) myeloma, and (c) leukemia, as set forth in claims 4 and 5, 6 and 7, and 8, respectively.

Claim 21 is generic to a plurality of distinct species of invention, wherein said autoimmune disease or disorder is selected from the group consisting of (d) rheumatoid arthritis and (e) systemic lupus erythrematosus, as set forth in claims 22 and 23, respectively.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of group I is the treatment of mammal having a neoplastic disease by a process comprising administering to the mammal a composition comprising a combination of two agents specific for either CD40 or CD20.

The special technical feature of group II is a kit.

The special technical feature of group III is the treatment of mammal having a autoimmune disease by a process comprising administering to the mammal a composition comprising a combination of two agents specific for either CD40 or CD20.

Accordingly, groups I-III are not linked by the same or corresponding special technical feature so as to form a single general inventive concept.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The special technical feature of each species of invention differs as each disease has a different etiology and pathology, and therefore the species are not so linked as to form a single general inventive concept.

Continuation of B. FIELDS SEARCHED Item 3:
MEDLINE, WEST: anti-CD20, anti-CD40, C2B8, S2C6, apoptosis, immunotherapy, antibody-mediated therapy, non-Hodgkins lymphoma, synergy, combination therapy